REMARKS

Applicants have amended claims 1, 2, 7, 10, 11, 12, 16, and 17 to more particularly point out and distinctly claim the subject matter of this invention. Support for the amendments can be found in the specification.[1] Note that the amendments have necessitates cancellation of claims 3-5, 8, 13-15,18-20, and 22. Cancellation of claim 22 has in turn necessitated change of the dependency of claim 23. No new matter has been introduced by the amendments.

Claims 1,2, 6, 7, 9-12, 16, 17, 21, 23, and 24 are now pending. Reconsideration of the application, as amended, is requested in view of the remarks below.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 1-3, 5-7, 9-13, 15-18, 20, 21, and 24 on the ground that the specification "does not reasonably provide enablement for the collagens when not partially digested." See the Office Action, page 2, lines 12-16. In particular, the Examiner pointed out that "[n]o method is described of preparing the collagens without partial digestion."

Applicants submit that this rejection has been overcome by the above amendments to claims 1, 2, 11, 12, 16, and 17.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 7 and 10 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. More specifically, the Examiner pointed out that "[t]he claims are unclear as to when in the method the cells and substrate are placed in the rotating and oscillating vessel."

Applicants have amended each of claims 7 and 10 to recite "during the growing step," and request withdrawal of this rejection.

---

[1] Amended claims 1, 11, and 16 each recite "partially digested type I collagen." Amended claims 2, 12, and 17 each recite "partially digested type II collagen." Support for these recitations can be found at page 5, lines 27-29. Claims 7 and 10, as amended, each recite "during the preparation step." Support for this recitation can be found at page 5, lines 27-29.

Rejection under 35 U.S.C. § 103 (a)

The Examiner rejected claims 1-6, 8, 9, and 11-24 as being unpatentable over Lai et al, U.S. Patent 5,876,444 ("Lai") in view of Muller et al., U.S. Patent 6,623,963 ("Muller") and Mansmann, U.S. Patent 6,530,956 ("Mansmann"). Among the rejected claims, claims 3-5, 8, 13-15, 18-20, and 22 have been canceled. Claims 1, 11, and 16 are independent claims and will be discussed first.

Claim 1 covers a method of fabricating a cartilage implant. The method includes (1) embedding chondrocytes or mesenchymal stem cells in a three-dimensional substrate containing randomly rewound α-helical monomers from partially digested type I collagen; and (2) growing the chondrocytes or mesenchymal stem cells in the substrate. Claim 11 covers a similar method in which chondrocytes, instead of chondrocytes or mesenchymal stem cells, are used. Claim 16 covers a cartilage implant which contains (1) a three-dimensional matrix containing randomly rewound α-helical monomers from partially digested type I collagen, and (2) chondrocytes embedded in the matrix. The patentability of claims 1, 11, and 16 resides at least in part in a three-dimensional substrate containing randomly rewound α-helical **monomers** of type I collagen.

Lai discloses a process of preparing a reconstituted collagen template for curing articular destruction. The process includes (1) uncoiling a triple-helical type I collagen to obtain α-helical monomers, (2) reducing residue disulfide bonds in the collagen to become –SH groups by utilizing mercaptoethanol, (3) cross-linking the α-helical monomers by utilizing glutaraldehyde, and (4) lyophilizing the cross-linked product to obtain the reconstituted collagen template.

The process disclosed in Lai includes cross-linking reaction between α-helical type I collagen monomers and glutaraldehyde. Products of this reaction are **polymers** containing two or more type I collagen monomers linked by $-CH(CH_2)_3CH-$ group. See column 4, lines 5-19 and Schemes III. In short, the reconstituted collagen template is made of **polymers**. Clearly, Lai does not teach or suggest a substrate made of α-helical type I collagen **monomers**. Neither Muller nor Mansmann cures this deficiency. Muller discloses a matrix containing a reconstituted type II collagen. The reconstituted type II collagen is also a cross-linked product, i.e., a

polymer. See column 3, lines 38-47. Mansmann discloses a scaffold for tissue repairing. The scaffold may be made of unmodified collagen (e.g., type I collagen or type II collagen). See column 8, lines 35-48, and column 14, lines 28-43. Note that native collagen has a triple-helical structure and, thus, is a **trimer**. Therefore, Lain, Muller, and Mansmann, alone or in combination, do not teach or suggest a substrate containing α-helical type I collagen **monomers**, a feature recited in claims 1, 11, and 16. In other words, the three references do not render claims 1, 11, and 16 obvious.

Claims 2, 6, and 9 depend from claim 1, claim 12 depends from claim 11, and claims 17, 21, 23, and 24 depends from claim 16. For the same reasons set forth above, these claims are also not rendered obvious over Lai in view of Muller and Mansmann.

CONCLUSION

Applicants submit that the grounds for rejection asserted by the Examiner have been overcome, and that claims 1, 2, 6, 7, 9-12, 16, 17, 21, 23, and 24, as pending, define subject matter that is definite, enabled, and nonobvious over the cited prior art references. On this basis, it is submitted that all claims are now in condition for allowance, an action of which is requested.

Please apply any charges to deposit account 06-1050.

Respectfully submitted,

Date: 1-6-04

Y. Rocky Tsao

Y. Rocky Tsao, Ph.D., J.D.
Attorney for Applicants
Reg. No. 34,053

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906